REMARKS

Claims 1-7 were pending in the application. Claims 1, 3, 4, and 7 have been amended. New Claim 39 has been added. Upon entry of these amendments, Claims 1-7 and 39 will be pending and under active consideration. Claims 1, 7, and 39 are independent.

Applicants submit respectfully that the amendments made herein are supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter.

The specification is amended to remove all instances of the term "http://" preceding internet addresses in order to eliminate all embedded hyperlinks and/or other form of browser-executable code, as required, under MPEP § 608.01, by Examiner at page 2 of the Office Action. Applicants submit respectfully that the internet addresses recited within the specification, as amended, are not hyperlinks or other browser-executable code.

Claims 1, 3, 4, and 7 are amended herein to better clarify the metes and bounds of Applicants' presently claimed invention. The amendments are supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter. In particular, the amendments to Claims 1, 3, 4, and 7 find support at page 3, line 30, to page 4, line 1, and page 20, line 26, to page 21, line 2, of the specification as filed.

New Claim 39 is added herein. Support for the added claim is found throughout the specification and claims as filed and, thus, the added claim does not represent new matter. In particular, support for Claim 39 is found in original Claim 8 and at page 3, line 30, to page 4, line 1, and page 20, line 26, to page 21, line 2, of the specification as filed.

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

I. The Rejections Under 35 U.S.C. § 102(b) Should Be Withdrawn

A. The Rejection Over McHugh Should Be Withdrawn

The Office Action, at pages 3-4, rejects Claims 1, 3, and 4-6 as allegedly being anticipated by McHugh (*Methods in Cell Biology* 1994, Chapter 33, Vol. 42, pages 575-595)(hereinafter, "McHugh"), under 35 U.S.C. § 102(b). The Office Action alleges that McHugh describes a technique of flow microsphere immunoassy for the simultaneous quantitation of several analytes in a sample through the use of a microsphere panel. In particular, the Office Action alleges that the different microsphere classes are coated with different capture reagents and the fluorescence associated with each microsphere class is quantitated with a flow cytometer, and the use of different microsphere classes, each coated with a different capture reagent, allows for the rapid and simultaneous detection of multiple analytes, allegedly as required by present Claim 1. Even further, the Office Action alleges that McHugh also describes the use of fluorescence as a descriptor of the microspheres, such that the microspheres can be separated by different fluorescent emissions at different concentrations, and that McHugh outlines that various studies have utilized a variety of capture reagents, such as antigens, antibody, receptors, immunoglobulins, oligonucleotides, proteins, DNA etc. Applicants traverse respectfully.

Applicants submit respectfully that Claims 1, 3, and 4-6, as amended, are not anticipated by McHugh because McHugh does not disclose each and every element of those amended claims

as is required for a *prima facie* showing of anticipation. In particular, Claim 1, as amended, is directed to a MAP Test Panel comprising 20 or more subsets of microspheres, the microspheres of one subset being distinguishable from those of another subset by their characteristic fluorescence signatures and harboring at least one reagent designed to interact selectively, if not specifically, with a predetermined analyte. As it is axiomatic in modern patent practice that elements recited within claims are interpreted in light of the specification, Applicants respectfully direct Examiner's attention to the recitations of page 3, line 29, to page 4, line 1, and page 20, lines 26-29, to define the expression "characteristic fluorescent signatures." As indicated in these passages, Applicants submit respectfully that a "characteristic fluorescent signature" derives from the incorporation of at least two fluorescent dyes into the microspheres of the present invention. A single dye is not described as providing a "characteristic fluorescent signature."

Applicants submit respectfully that McHugh does not teach or suggest a microsphere having a "characteristic fluorescent signature" as defined by Applicants. As noted by Examiner, McHugh teaches the use of fluorescence as a descriptor of the microspheres, such that the microspheres can be separated by different fluorescent emissions at different concentrations. However, McHugh does not teach or suggest the use of multiple fluorescent dyes incorporated into single microspheres to create a "characteristic fluorescent signature" as defined by Applicants. Hence, Applicants submit respectfully that McHugh does not disclose, either explicitly or inherently, each and every element of Applicants' claimed invention.

Accordingly, Applicants request respectfully that the rejection to Claims 1, 3, and 4-6 under 35 U.S.C. § 102(b) be withdrawn.

B. The Rejection Over Kettman Should Be Withdrawn

The Office Action, at page 4, rejects Claims 1, 3, and 4-6 as allegedly being anticipated by Kettman *et al.* (Cytometry 1998, Vol.33, pages 234-243)(hereinafter, "Kettman") under 35 U.S.C. § 102(b). The Office Action alleges that Kettman teaches a method and system for analysis of multiple analytes in a single sample using a set of microspheres identifiable by characteristic fluorophores embedded in the particles. Applicants traverse respectfully.

Without acquiescing in the propriety of the rejection, Applicants submit respectfully that Kettman is not a proper reference under 35 U.S.C. § 102(b). The priority date of the present application is September 15, 1999, and the date of publication of Kettman, as reported at the publisher's website (www3.interscience.wiley.com) is October 1, 1998. Hence, Applicants submit that Kettman was not publicly available more than one year prior to Applicants' priority date.

Applicant submits respectfully that the claims of the present invention, as amended, are not anticipated by Kettman under 35 U.S.C. § 102(b). Accordingly, Applicant requests respectfully that the rejection of Claims 1, 3, and 4-6 under 35 U.S.C. § 102(b) be withdrawn.

C. The Rejection Over WO 99/19515 Should Be Withdrawn

At page 5 of the Office Action, Claims 1-7 are rejected under 35 U.S.C. § 102(b) as being anticipated by published PCT application WO 99/19515, publication date April 22, 1999. The Office Action alleges that WO 99/19515 teaches a population of subsets of dyed beads in batches, each one of them having a predetermined ratio or proportion of two or more fluorescent dyes, thus forming a set having optically distinct microspheres useful for

simultaneous analysis of a plurality of analytes in the same sample. Applicants traverse respectfully.

As noted above, the priority date claimed for the present application is September 15, 1999. Therefore, Applicants submit respectfully that WO 99/19515 is not a proper 35 U.S.C. § 102(b) reference.

However, the Office Action asserts at page 5 that, although Applicants' claim for domestic priority under 35 U.S.C. 119(e) is acknowledged, the provisional application upon which priority is claimed allegedly fails to provide adequate support under 35 U.S.C. § 112 for Claims 1-7 of the present application. The Office Action alleges that, while Claims 1-7 are drawn to a Multi-Analyte Profile Test Panel, provisional application 60/153,941 only mentions the MAP Test Panel but allegedly does not provide a detailed description of the Panel such that one skilled in the art could use or make it. Applicants traverse respectfully.

Applicants submit respectfully that provisional application 60/153,941 does indeed provide adequate written description to support the MAP Test Panel of the present invention. Applicants submit respectfully that provisional application 60/153,941, at page 5, last full paragraph, incorporates the necessary teaching by reference to several published PCT patent applications; WO 99/19515, which is alleged in the present Office action to be a 35 U.S.C. § 102(b) reference against the present application, is among these. While acknowledging that provisional application 60/153,941 does not actually recite the express phrase, "these documents are incorporated by reference," Applicants submit respectfully that such a recitation is not absolutely required for incorporation of essential material into a provisional application. As recited at page 5, lines 14-16, "the level of biochemical screening proposed for this project can only be performed by technology developed by Luminex Corporation and disclosed as published

patent applications: [Applicants' list of references]." (Emphasis added). Thus, by inclusion of the term "only" in the reference to those applications, Applicants direct one skilled in the art inexorably to the documents containing the necessary description to practice the present invention.

Furthermore, as Applicants are among the inventors of the referenced applications, there can be little doubt that the methods by which the present invention is practiced, as disclosed within the references, were in the possession of the present Applicants as of the claimed priority date.

Respectfully, Applicants direct Examiner's attention to 37 C.F.R. § 608.01(p)(I)(B), which provides the standard for incorporation by reference in applications which are relied upon to establish an earlier effective filing date. The C.F.R. notes that "an application is entitled to rely upon the filing date of an earlier application, even if the earlier application itself incorporates essential material by reference to another document." Also, "[N]either 35 U.S.C. § 119(a) nor 35 U.S.C. § 120 places any restrictions as to how the claimed invention must be disclosed in the earlier application to comply with 35 U.S.C. § 112, first paragraph. Accordingly, Applicants submit respectfully that provisional application 60/153,941 makes reference to patent applications that provide the necessary teaching to practice the presently claimed invention as provided under 37 C.F.R. § 608.01(p)(I)(B).

In view of the above, Applicants submit respectfully that the present application is entitled to the claimed priority date of September 15, 1999. Accordingly, Applicants submit respectfully that WO 99/19515 is not a proper 35 U.S.C. § 102(b) reference, and Applicants respectfully request that the 35 U.S.C. § 102(b) rejection of Claims 1-7 be withdrawn.

II. Rejections Under 35 U.S.C. § 112, Second Paragraph

At pages 2-3 of the Office Action, Claims 1-7 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out particularly and claim distinctly the subject matter regarded as the invention. The Office Action alleges that the claims, Claim 1 in particular, do not adequately describe how the microspheres of one subset used in the claimed invention are distinguishable from the microspheres of another subset. Applicants traverse respectfully.

Applicants submit respectfully that Claims 1-7, in particular Claim 1, as amended, are clear and definite in their description. Claim 1 recites that "microspheres of one subset being distinguishable from those of another subset by their characteristic fluorescence signatures." (Emphasis added). As noted above, the meaning of the term "characteristic fluorescence signature" is described within the specification as filed at page 3, line 29, to page 4, line 1, and page 20, lines 26-29, and clearly defines the means by which subsets of microspheres are distinguished. On this basis, Applicants suggest respectfully that the rejection has been overcome, and Applicants request respectfully that the 35 U.S.C. § 112, second paragraph, rejection of Claims 1-7 be withdrawn.

III. The Objection To The Claims Should Be Withdrawn

At page 2, the Office Action objects to Claim 7 under 37 C.F.R. § 1.75 as allegedly being a substantial duplicate of Claim 1. The Office Action alleges that Claims 1 and 7 are directed to the same Test Panel, and that the insertion of "kit" in the preamble does not change the structural or functional limitations of these claims. Applicants traverse respectfully.

Applicants submit respectfully that Claims 1 and 7 are not substantial duplicates. Applicants submit respectfully that a kit for assaying multiple analytes in a single pass through a flow analyzer comprising a Multi-Analyte Profile (MAP) Test Panel is patentably distinct from the MAP itself. Respectfully, Applicants direct Examiner's attention to page 21, lines 1-2, which describe how kits may be prepared comprising the MAP Test Panel and associated buffers, vials and supplemental reagents. Thus, a kit is disclosed in the present specification to one skilled in the art as potentially containing a number of other items in addition to the MAP Test Panel, itself. Accordingly, Applicants request respectfully that the objection to Claims 1 and 7 be withdrawn.

CONCLUSION

Applicants submit respectfully that the present application is in condition for allowance. Favorable reconsideration, withdrawal of the rejections set forth in the above-noted Office Action, and an early Notice of Allowance are requested.

Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3500. All correspondence should be directed to our address given below.

AUTHORIZATION

Applicants believe there is no fee due in connection with this filing. However, to the extent required, the Commissioner is hereby authorized to charge any fees due in connection with this filing to Deposit Account 50-1710 or credit any overpayment to same.

Respectfully submitted,

Gilberto M. Villacorta, PH.D.
Registration No. 34,038
Serge Sira
Registration No. 39,445
Robert R. Seabold, PH.D.
Registration No. 41,298

Patent Administrator
KATTEN MUCHIN ZAVIS ROSENMAN
525 West Monroe Street, Suite 1600
Chicago, Illinois 60661-3693
Facsimile: (312) 902-1061

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http://www.cybergenome.com/tools/databases.htm;

http://www.genome.ad.jp/manuscripts/GIW94/Poster/GIW94P06.html;

http://www2.links2go.com/topic/Protein_Databases;

http://www.biochemie.net/links/Databases/Protein/;

http://www.bioscience.org/urllists/protdb.htm; and

http://www.gcrdb.uthscsa.edu/help_files/fast_doc.html, among many others.

For the purpose of facilitating the selection of required reagents, the contents of these databases and updates thereof should be used advantageously.

Furthermore, one can easily make antibodies or binding pairs against any of these proteins. Also, antibodies against some of these proteins are readily available. For example, the publication on http://gbsl.freeservers.com provides more than 1900 monoclonal antibodies, including anti-idiotype, bispecific, human, chimeric, diabodies, single chain Fv, etc. The MSRS (Manufacturers' Specifications and Reference Synopsis) Primary Antibody Database is an online reference source that lists over 76,000 monoclonal and polyclonal primary antibodies. The URL is http://www.antibodies-probes.com.

Of course, one can order custom-made antibodies from various commercial manufacturers. The http://www.antibodyresource.com website provides an exhaustive list of companies making and/or selling such reagents: Bethyl Laboratories - (polyclonal, peptides); AbCam Ltd - (monoclonal, polyclonal); Advanced ChemTech - (polyclonal, peptides); AgriSera AB - (monoclonal, polyclonal, peptides); Anaspec - (polyclonal, peptides); Anawa Trading Company SA - (monoclonal, polyclonal, peptides); Antibody Solutions - (monoclonal, polyclonal, peptides) - in vitro production; Affiniti Research Products Ltd. - (UK) - (polyclonal, peptides); Affinity BioReagents, Inc. - (polyclonal); Alpha Diagnostics - (monoclonal, polyclonal, peptides); Antibodies Incorporated - (monoclonal, polyclonal); Aurora Biomolecules - (polyclonal, peptides); Aves Lab - (polyclonal) - chicken antibodies; B & K Universal, Ltd. - (monoclonal, peptides); Berkeley Antibody Company - (monoclonal, polyclonal); BIOCON, Inc. - (monoclonal, polyclonal)- in vitro; BioDiversa - (monoclonal, polyclonal, peptides); Biogenes - (monoclonal, polyclonal, peptides); Biogenesis - (monoclonal, polyclonal, peptides); Bio-Express - (monoclonal) - in vitro and IgG fragment production; Bioinvent International AB - (monoclonal) - human monoclonal antibodies; Bionostics, Inc. - (monoclonal, polyclonal); Bioquest - (monoclonal, polyclonal); BioSource International - (monoclonal, polyclonal); Bio-Synthesis - (monoclonal, polyclonal, peptides); Biotrend - (monoclonal, polyclonal, peptides); Biovendor - (monoclonal, polyclonal); Bioworld - (monoclonal, polyclonal, peptides); Babraham

lipids, and viruses, to name a few) and haptens, which may be rendered antigenic under suitable conditions and recognized by antibodies or antibody fragments.

The present method is useful for the detection and analysis of a wide variety of analytes. The term "analyte" is meant to be construed broadly and includes "antigens," "antibodies," "enzymes," "nucleic acids,"and the like. but is not solely limited to "antigens". Many types of analytes are conceived, including, for example, environmental contaminant analytes, agricultural products, industrial chemicals, water treatment polymers, pharmaceutical drugs, drugs of abuse, and biological analytes, such as antigenic determinants of proteins, polysaccharides, glycoproteins, lipoproteins, nucleic acids, hormones, and parts of organisms, such as viruses, bacteria, fungi, parasites, plants and microbes.

The term "reagent" refers to the reaction partner or binding partner of an analyte. The molecular interactions between reagent and analyte are generally selective, preferably specific. Preferred analyte:reagent (or vice-versa) couples, however, include, but are not limited to, antigen:specific immunoglobulin; hormone:hormone receptor; nucleic acid strand:complementary polynucleotide strand; avidin:biotin; protein A:immunoglobulin; protein G:IgG immunoglobulins; enzyme:substrate; lectin:specific carbohydrate; drug:protein; small molecule:protein, and the like.

Known and unknown analytes, such as proteins, present in a clinical sample can be obtained by purification to serve as a reference material. Synthetic or recombinant peptides, polypeptides and proteins can also be prepared from the sequence information from any of a number of publicly accessible protein databases, including those available on the Internet. For example, such databases include PubMed, SwissProt, PIR, PRF, PDB, and translations from annotated coding regions in GenBank and RefSeq (~~http://~~www.ncbi.nlm.nih.gov/PubMed). Other Internet sites with protein databases, suitable for retrieving sequences of proteins or their fragments, include:

~~http://~~www.kazusa.or.jp/huge/;

~~http://~~alces.med.umn.edu/dbmotif.html;

~~http://~~www.harefield.nthames.nhs.uk/nhli/protein/other_sites.html;

~~http://~~www.biomed.man.ac.uk/ugrad/biomedical/calpage/sproject/alf/biodb.html;

~~http://~~sphinx.rug.ac.be:8080/other2D.html;

~~http://~~discover.nci.nih.gov/host/prot.html;

~~http://~~www.infobiogen.fr/services/dbcat/data/dbcat_PROT.html;

~~http://~~www.infobiogen.fr/services/deambulum/english/db4.html;